MAYO CLINIC
Mayo Medical Laboratories

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# Unit Code 83050: Alpha-1-Antitrypsin Deficiency Profile

## Useful For

This is Mayo's preferred approach for diagnosing alpha-1-antitrypsin deficiency (alpha-1-antitrypsin quantitation and genotype)

Determining the specific allelic variant (genotyping) for prognosis and genetic counseling

## Genetics Test Information

Profile includes serum alpha-1-antitrypsin levels and molecular analysis (S and Z alleles). If the genotyping and quantitative serum level are discordant, #17089 "Alpha-1-Antitrypsin (A1A) Phenotyping, Serum" will be added and performed at an additional charge.

## Profile Information

| Unit Code | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| 82993 | Alpha-1-Antitrypsin Genotyping, B | No | Yes |
| 17088 | Alpha-1-Antitrypsin, S | Yes (order #8161) | Yes |

## Reflex Tests

| Unit Code | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| **17089** | A1AT Phenotype, S | Yes (order #26953) | No |

## Testing Algorithm

If the genotyping and quantitative serum level are discordant, then #17089 Alpha-1-Antitrypsin (A1A) Phenotyping, Serum will be added and performed at an additional charge.

## Special Instructions and Forms

| | |
|---|---|
| • | **Molecular Genetics-Congenital Inherited Diseases Patient Information Sheet** |
| • | **Informed Consent for Genetic Testing** |
| • | **Alpha-1-Antitrypsin-A Comprehensive Testing Algorithm** |
| • | **Alpha-1-Antitrypsin Reflex Table** |

## Method Name

82993: Polymerase Chain Reaction (PCR)
(PCR is utilized pursuant to a license agreement
with Roche Molecular Systems, Inc.)
17088: Nephelometry
17089: Isoelectric Focusing
General Information:
See "Alpha-1-Antitrypsin-A Comprehensive Testing Algorithm" in Special Instructions.

## Reporting Name

A1AT Deficiency Profile

## Ordering Mnemonic

A1ATPR

## Aliases

A-1-Antitrypsin
A1A
AAT (Alpha-1-Antitrypsin)
Alpha 1 Antitrypsin
Alpha one Antitrypsin
Alpha1-Proteinase Inhibitor (Prolastin)
Anti-Alpha-1-Trypsin
Antitrypsin
Phenotype
Phenotyping
Pi Typing
Prolastin (Alpha1-Proteinase Inhibitor)
Protease Inhibitor Allo Typing
SERPINA1
Soft-A1ATR

## Specimen Type

Mixed

## Specimen Required

**Blood and serum are required.**

**Specimen must arrive within 96 hours of draw.**

**Blood**
**Container/Tube:** Lavender-top (EDTA) tube or yellow-top (ACD) tube
**Specimen Volume:** 2.5 mL of whole blood
**Forms:** Molecular Genetics-Congenital Inherited Diseases Patient Information Sheet (Supply T521)
**Note: New York Clients-Informed consent is required.** Please document on the request form or electronic order that a copy is on file. An Informed Consent for Genetic Testing (Supply T576) is available.
See Special Instructions for a copy of these forms.
**Collection Instructions:** Invert several times to mix blood. Send specimen in original tube.
**Note:** Label specimen appropriately (blood).

**Serum**
**Container/Tube:** Plain, red-top tube or serum gel tube
**Specimen Volume:** 1 mL of serum
**Collection Instructions:**
**Note:** Label specimen appropriately (serum).

## Specimen Minimum Volume

Blood: 0.5 mL
Serum: 0.5 mL

## Reject Due To

| | |
|---|---|
| Specimens Other Than: | Whole blood and serum |
| Anticoagulants Other Than: | EDTA, ACD preferred - any anticoagulant acceptable |
| Hemolysis: | NA |
| Thawing: | Warm OK; Cold OK |
| Lipemia: | NA |
| Icteric: | NA |

## Transport Temperature

Varies
Ambient\Refrig OK\Frozen NO-Blood
Refrig <14 days\Frozen <14 days OK\Ambient <3 days OK-Serum

## Clinical Information

Alpha-1-antitrypsin (A1A) is a protein that inhibits the enzyme neutrophil elastase. It is predominantly synthesized in the liver and secreted into the bloodstream. The inhibition function is especially important in the lungs because it protects against excess tissue degradation. Tissue degradation due to A1A deficiency is associated with an increased risk for early onset panlobar emphysema, which initially affects the lung bases (as opposed to smoking related emphysema, which presents with upper lung field emphysema). Patients may become symptomatic in their 30's and 40's. The most frequent symptoms reported in a National Institute of Health study of 1,129 patients with severe deficiency (mean age 46 years) included cough (42%), wheezing (65%), and dyspnea with exertion (84%). Many

patients were misdiagnosed as having asthma. It is estimated that approximately one sixth of all lung transplants are for A1A deficiency. Liver disease can also occur, particularly in children; it occurs much less commonly than emphysema in adults.

A1A deficiency is a relatively common disorder in Northern European Caucasians. The diagnosis of A1A deficiency is initially made by quantitation of protein levels in serum followed by determination of specific allelic variants by isoelectric focusing (IEF). While there are many different alleles in this gene, only 3 are common. The 3 major alleles include: M (full functioning, normal allele), S (associated with reduced levels of protein), and Z (disease-causing mutation associated with liver disease and premature emphysema). The S and Z alleles account for the majority of the abnormal alleles detected in affected patients. As a codominant disorder, both alleles are expressed. An individual of SZ or S-null genotype may have a small increased risk for emphysema (but not liver disease) due to slightly reduced protein levels. On the other hand, an individual with the ZZ genotype is at greater risk for early onset liver disease and premature emphysema. Smoking appears to hasten development of emphysema by 10 to 15 years. These individuals should be monitored closely for lung and liver function.

Historically, IEF has been the primary method for characterizing variants, though in some cases the interpretation is difficult and prone to error. Serum quantitation is helpful in establishing a diagnosis but can be influenced by other factors. DNA-based assays are routinely used to test for deficiency alleles, but can miss disease alleles other than the S and Z alleles. This test combines all of these methods to provide a comprehensive result. See "Alpha-1-Antitrypsin-A Comprehensive Testing Algorithm" in Special Instructions.

## Reference Values

ALPHA-1-ANTITRYPSIN GENOTYPING
An interpretive report will be provided.
ALPHA-1-ANTITRYPSIN
100-190 mg/dL

## Interpretation

For each of the possible alpha-1-antitrypsin (A1A) genotypes there is an expected range for the total serum level of A1A. However, a number of factors can influence either the A1A serum level or the A1A genotype results, including acute illness (A1A is an acute phase reactant), protein replacement therapy, the presence of other rare variants and/or the presence of DNA polymorphisms. When the serum level differs from what is expected for that genotype (ie, discordant), additional studies are performed to ensure the most appropriate interpretation of test results. Additional follow-up may include A1A phenotyping by isoelectric focusing, obtaining additional clinical information, and DNA sequencing. See "Alpha-1-Antitrypsin Reflex Table" in Special Instructions.

## Cautions

This assay will not detect all of the mutations that cause alpha-1-antitrypsin (A1A) deficiency. Therefore, the absence of a detectable mutation(s) does not rule out the possibility that an individual is a carrier of or affected with this disease.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

In rare cases, DNA alterations of undetermined significance may be identified.

A previous bone marrow transplant from an allogenic donor will interfere with testing. Call Mayo Medical Laboratories for instructions for testing patients who have received a bone marrow transplant.

## Clinical Reference

1. Stoller JK, Aboussouan LS: Alpha-1-antitrypsin deficiency. Lancet 2005; 365:2225-2236.
2. McElvaney NG, Stoller JK, Buist AS, et al: Baseline characteristics of enrollees in the National Heart, Lung and Blood Institute Registry of alpha 1-antitrypsin deficiency. Alpha 1-Antitrypsin Deficiency Registry Study Group. Chest 1997;111:394-403
3. Snyder MR, Katzmann JA, Butz ML, et al: Diagnosis of alpha-1-antitrypsin deficiency: an algorithm of quantification, genotyping, and phenotyping. Clin Chem 2006;52:2236-2242

## Method Description

A PCR-based assay is used to detect the Z and S allele within the alpha-1-antitrypsin (A1A) *SERPINA1* gene. Other A1A variants will not be detected by this assay. A1A serum levels are measured by immunonephelometry. The serum level will be reported with the genotyping result. Any genotyping results that are discordant with the serum level will be phenotyped by isoelectric focusing. (Pierce JA: Hereditary pulmonary emphysema. In Emery and Rimoin's Principles and Practices of Medical Genetics. Vol. 2. 3rd edition. Edited by DL Rimoin, JM Connor, RE Pyeritz. New York, Churchill Livingstone, 1997, pp 2727-2750; instruction manual: Behring  Nephelometer II. Dade Behring, Inc., Newark, DE)

## Day(s) and Time(s) Test Performed

Monday, Wednesday; 2 pm

## Analytic Time

5 days

## Maximum Laboratory Time

7 days

## Specimen Retention Time

See Individual Unit Codes

## Performing Laboratory Location

Rochester

## CPT Code Information

82103-Alpha-1-antitrypsin
83890-Molecular isolation or extraction
83896 x 2-Nucleic acid probe, each
83898 x 2-Amplification, target, each nucleic acid sequence

83912-Interpretation and report
82104-Alpha-1-antitrypsin phenotype (if appropriate)